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1 510(k) Summary

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Idaho Technology Inc. JBAIDS Anthrax Detection System

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

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Date Prepared: November 14, 2005

Device Name: Trade Name:

JBAIDS Anthrax Detection System

Common Name:

Real-time PCR amplification and detection system for targeted *Bacillus anthracis* DNA sequences

Classification Name:

System: Microorganism differentiation and identification device; 21 CFR 866.2660

Instrument: Micro Chemistry Analyzer for Clinical Use; 21 CFR 862.2170, product code JJF

Reagent Kit: (*B. anthracis*) Unclassified

Device Description:

The Joint Biological Agent Identification and Diagnostic System (JBAIDS) Anthrax Detection System is a fully integrated *in-vitro* diagnostic (IVD) system composed of the JBAIDS instrument with laptop computer, software, 2 different freeze-dried reagent assays (in one kit) for the qualitative detection of pathogenic *Bacillus anthracis,* and 3 different sample preparation protocols for isolating target DNA from whole blood, blood culture, or direct culture.

The JBAIDS instrument, using Polymerase Chain Reaction (PCR) technology, is a portable thermocycler and real-time fluorimeter. The *JBAIDS Anthrax Detection Kit* is specially designed for PCR in glass capillaries using the JBAIDS instrument and hydrolysis probes for detection of the pXO1 plasmid (Target 1) and the pXO2 plasmid (Target 2) DNA sequences. A fragment of plasmid DNA is amplified using specific primers, creating amplicon. The amplicon is detected using a specific hydrolysis probe, which is a short oligonucleotide that hybridizes to an internal sequence of the amplified fragment during the annealing phase of the PCR cycle. This probe has the 5' and 3' ends labeled with a reporter dye and a quenching dye, respectively. When the probe hybridizes to the specific DNA target, the Taq polymerase enzyme replicating the target-specific DNA hydrolyzes the probe, separating the two fluorophores, thus allowing the reporter dye to fluoresce.

The reagent kit contains 4 different types of freeze-dried reagent vials: Positive Controls, Negative Controls, Inhibition Controls, and Unknowns (used for testing the patient sample). Each JBAIDS run requires a Positive and Negative Control, and each sample is tested using both an Inhibition Control vial and an Unknown reagent vial. The characteristics of the amplification curves from the positive control (PC), negative control (NC), inhibition controls (IC) and from each unknown sample are analyzed by the JBAIDS Software, and results are reported as Positive, Negative, Inhibited or Uncertain. When PCs or NCs are unacceptable, the test results for all samples in the JBAIDS run are considered invalid and must be repeated.

Prior to testing, whole-blood samples are purified using the Idaho Technology IT *1-2-3*™ FLOW Sample Purification Kit (or validated equivalent), while blood culture and direct culture specimens are prepared using the IT *1-2-3*™ SWIPE Sample Purification Kit (or validated equivalent). The resulting purified sample is added to an Unknown reagent vial and an Inhibition Control reagent vial, along with reconstitution buffer.

Intended Use: The JBAIDS Anthrax Detection System is a real-time polymerase chain reaction (PCR) test system intended for the qualitative *in vitro* diagnostic (IVD) detection of target DNA sequences on the pXO1 plasmid (Target 1) and the pXO2 plasmid (Target 2) from *Bacillus anthracis*. The system can be used to test human whole blood collected in sodium citrate from individuals suspected of having anthrax, positive blood cultures, and cultured organisms grown on blood agar plates. The JBAIDS Anthrax Target 2 assay is used as a supplementary test only after a positive result with the Target 1 Assay.

The JBAIDS Anthrax Target 1 and Target 2 Assays are run on the JBAIDS instrument using the Diagnostic Wizard.

Results are for the presumptive identification of *B. anthracis*, in conjunction with culture and other laboratory tests. The following considerations also apply:

- The diagnosis of anthrax infection must be made based on history, signs, symptoms, exposure likelihood, other laboratory evidence, in addition to the identification of pXO1 and pXO2 targets either from cultures or from direct blood specimens.
- The assays have not been evaluated with blood from individuals without clinical signs or symptoms who were presumed exposed and who subsequently developed anthrax (inhalation or other forms of the disease), or from individuals with any form of anthrax (inhalational, cutaneous, or gastrointestinal).
- The level of plasmid targets that would be present in blood from individuals with early systemic infection is unknown.
- The definitive identification of *B. anthracis* from colony growth, liquid blood culture growth, or from blood specimens requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reports are required.

The safety and effectiveness of other types of tests or sample types (not identified as "For in vitro diagnostic use") have not been established.

Substantial Equivalence: The JBAIDS Anthrax Detection System is substantially equivalent to other products in commercial distribution intended for similar use. The JBAIDS instrument is substantially equivalent to the currently marketed LightCycler® Instrument Version 1.2, cleared under K033734.

The predicate for the JBAIDS Anthrax Detection Kit is traditional microbiological identification of the organism (preamendment methods) with confirmation by the Centers for Disease Control Laboratory Response Network Gamma Phage Lysis assay.

The following tables compare the JBAIDS Anthrax Detection System with the predicate devices, the LightCycler and classical microbiology.

Table1. JBAIDS Instrument System vs. LightCycler®

ELEMENT	NEW PRODUCT: JBAIDS Anthrax Detection System	PREDICATE: LightCycler® (K033734)
Intended Use	The JBAIDS instrument system is a ruggedized automated real-time PCR amplification and detection system for nucleic acids using fluorescence detection capable of simultaneous and rapid identification of multiple microbiological agents from a variety of biological specimens. The JBAIDS is intended for use by personnel trained in laboratory techniques and on the use of the analyzer. For this application, the intended use is for detection and identification of *B. anthracis* in whole blood, blood culture or direct culture from patients suspected of having anthrax.	The LightCycler® Instrument is a fully automated amplification and detection system for nucleic acids using fluorescence detection. The LightCycler® is intended to be used by laboratory professionals trained in laboratory techniques and on the use of the Analyzer.
Primary Operational Components	Integrated thermocycler and microvolume fluorimeter for walk-away PCR amplification and detection	Same
Detection Procedure	Optical detection of stimulated fluorescence	Same
Specimen Type	Purified nucleic acids	Same
Specimen Preparation	Performed off-line	Same
Temperature Range	30-99 °C	40-98 °C
User Interface	Ruggedized laptop with instrument-specific software (JBAIDS version 2.1 or higher)	Laptop with instrument-specific software (LightCycler® version 3.5 or higher)
Heating Method Thermal Cycling	Hot-air cycling with glass capillaries	Same
Number of Thermal Cyclers	One	Same

ELEMENT	NEW PRODUCT: JBAIDS Anthrax Detection System	PREDICATE: LightCycler® (K033734)
Capillary Positions	32	Same
Reaction Size	5-20 µL in glass capillaries	10-20 µL in glass capillaries
Number of Optical Detection Channels	Three with fixed wavelengths (530 nm, 640 nm, 710 nm)	Same
Detection Chemistry	Paired hybridization probes, hydrolysis probes (i.e. TaqMan™), double stranded DNA binding dyes.	Same
Detection Timing	Detection occurs at defined intervals during PCR cycle and can be viewed in real time.	Same

The JBAIDS instrument has technological characteristics nearly identical to those of the LightCycler, with the addition of ruggedization for the military environment. The JBAIDS instrument raises no new issues with respect to safety or effectiveness.

The predicate instrument (Roche LightCycler®) has been used by the Centers for Disease Control and Prevention (CDC) Laboratory Response Network for the detection of *B. anthracis*. The CDC reported high sensitivity and specificity for *B. anthracis* detection with the predicate device when used with a 5' nuclease probe.[1] The LightCycler® has also been used to detect *B. anthracis* using HybProbe™ probes with high sensitivity and specificity.[2]

Table2. JBAIDS Anthrax Detection System vs. Microbiological Identification

ELEMENT	NEW PRODUCT: JBAIDS Anthrax Detection System	PREDICATE: Microbiological Identification (Preamendment Device)
Intended Use	Qualitative *in vitro* diagnostic (IVD) detection of target DNA sequences on the pXO1 plasmid (Target 1) and the pXO2 plasmid (Target 2) from *Bacillus anthracis.* Results are used in conjunction with clinical information, culture, and other laboratory tests as an aid in the diagnosis of anthrax infection in individuals suspected of having the disease.	Identification of anthrax infection through clinical information and standard microbiology techniques, including morphologic characteristics, and confirmed with CDC's Laboratory Response Network (LRN) gamma phage lysis assay (CDC catalog #BP3123) Presumptive and confirmatory identification is outlined in CDC publication, *Reference Laboratory General Procedure for Identification of* Bacillus anthracis, "Table 2, *B. anthracis* presumptive and confirmatory identification criteria" (see Appendix F.3).
Specimen	Whole blood (collected in 3.2% sodium citrate), blood culture (grown in soybean-casein digest broth), or bacterial culture (grown on blood agar)	Whole blood or blood culture plated for isolation of cells; sample is the growth from isolated colony/pure culture.
Specimen Preparation	Purified with IT *1-2-3*™ FLOW Sample Purification Kit or IT *1-2-3*™ SWIPE Sample Purification Kit (or validated equivalent)	Grown overnight on sheep blood agar plate inoculated with gamma phage
Time Required for Analysis of Specimen	Less than 3 hours	16-20 hours after obtaining isolated colony; approximately 3 days after first obtaining a patient sample
Physical Properties	Freeze dried reagents with reconstitution water and buffer provided in kit	Stock suspension (phage) plus blood agar plates
Test Result	Identification of 2 plasmids required for pathogenicity of the organism; both plasmids are found together in virulent strains of *B. anthracis.*	Identification of *B. anthracis.* Pathogenicity of the organism is based on patient symptoms and is not determined by laboratory methods.
Storage and Shelf Life	Six months at room temperature (18-28 °C)	2-8°C; phage viability decreases over time and can be reduced or destroyed by contaminants.

Gamma phage is a specific bacterial virus used in the CDC Laboratory Response Network Gamma Phage Lysis Assay as an IVD culture plating method to distinguish *B. anthracis* from *B. cereus* and other *Bacillus* species. Lawns of suspected *B. anthracis* are inoculated with gamma phage. Clear or partially clear zones of bacterial lysis are indicative of *B. anthracis.* The result from this test is used in conjunction with culture

and other laboratory tests and clinical information as an aid in the diagnosis of systemic anthrax infection in individuals suspected of having the disease.

The JBAIDS Anthrax Detection System is intended for the qualitative IVD detection of targeted DNA sequences on the pX01 plasmid (Target 1) and the pX02 plasmid (Target 2) from the *B. anthracis* pathogen, both of which are essential for the organism's pathogenicity. The system can be used to test human whole blood collected in sodium citrate tubes, positive blood cultures, and cultured organisms grown on blood agar plates. The results from the PCR tests are used in conjunction with culture and other laboratory tests and clinical information as an aid in the diagnosis of systemic anthrax infection in individuals suspected of having the disease.

The preamendment predicate device and the JBAIDS system have the same intended use; they both provide test results that aid in the diagnosis of anthrax when considered with other clinical and microbiological evidence.

The JBAIDS Anthrax Detection System yielded positive results with both the Target 1 and Target 2 assays for 23/23 (100%) of the isolates included in the direct culture panel, and for 11/11 (100%) of the isolates included in the blood culture panel. For the direct culture and blood culture panels, all of the samples were confirmed as *B. anthracis* using standard biochemical identification and tested positive using the CDC Reference Laboratory Procedure for Identification of *B. anthracis* Using Lysis by Gamma Phage. In addition 67/68 (98.5%) whole blood samples spiked with limit of detection levels of live *B. anthracis* were correctly identified by the JBAIDS assay.

The analytic specificity evaluation of the JBAIDS Anthrax Detection System was conducted with organisms that are phylogenetically related to *B. anthracis*, as well as with unrelated organisms that are likely to be found in clinical samples.

Regardless of the sample matrix, the JBAIDS Anthrax Detection System gave positive test results with both the Target 1 and Target 2 assays for all virulent strains of *B. anthracis* tested.

- 23 of 23 virulent strains of *B. anthracis* included in the direct culture panel were detected by both assays.
- 11 of 11 virulent strains of *B. anthracis* included in the blood culture panel were detected by both assays.

The JBAIDS Anthrax Detection System assays also proved to be very specific.

- 34* of 37 non-*B. anthracis* strains tested in the direct culture panel were negative for both the Target 1 and Target 2 assays. This included 25 phylogenetically related organisms and 12 unrelated organisms that might be found in clinical samples.
- 12 of 12 non-*B. anthracis* strains tested in the blood culture panel yielded negative results with both the Target 1 and Target 2 assays. This testing panel included 2 phylogenetically related organisms and 10 unrelated organisms that might be found in clinical samples.

*The assay did cross-react with 3 virulent forms of *B. cereus;* however, these specific isolates have been known to cause anthrax-like illnesses.[3]

In addition to analytic studies, a multi-site clinical trial was conducted. Due to the near absence of clinical samples from individuals with a diagnosis of systemic anthrax, the clinical trial was limited to an assessment of the system's clinical specificity. Blood samples from hospitalized subjects with clinical signs and symptoms consistent with

inhalation or systemic anthrax and for whom a blood culture had been ordered, were tested for *B. anthracis* using the JBAIDS Anthrax Detection System and the results compared to the gold standard technique of blood culture. All 150 subject samples yielded negative test results using the JBAIDS Anthrax Detection system and *B. anthracis* was not identified in any of the blood cultures. The clinical specificity of the JBAIDS Anthrax Detection System is 100% (95% CI, 98%-100%).

Based on the available gamma phage literature and this study, the JBAIDS Anthrax Detection System appears to be as effective as the predicate assay. The JBAIDS software automatically interprets the assay results, reducing the opportunity for user error, and the freeze-dried assay format minimizes assay setup errors. An additional practical and safety advantage of the JBAIDS Anthrax Detection System over the predicate comes from the nature of the positive controls of the two assays. The gamma phage assay requires live, nonvirulent *B. anthracis* while the JBAIDS system uses only nucleic acid as a positive control.

In summary the JBAIDS assay, while technologically distinct from the predicate, is as safe and effective as the predicate, is easier to use, and is highly sensitive and specific.

References

1 Hoffmaster AF, Meyer RF, Bowen M, Marston CK, Weyant RS, Thurman K, et al. Evaluation and validation of a real-time polymerase chain reaction assay for rapid identification of Bacillus anthracis. *Emerg Infect Dis* [serial online] 2002;Oct:8. Available from: URL: http://www.cdc.gov/ncidod/EID/vol8no10/02-0393.htm.

2 Bell, CA, et al. Detection of *Bacillus anthracis* DNA by LightCycler PCR. *J Clin Microbiol*. 2002;40:2897-2902.

3 Hoffmaster AR, Ravel J, Rasko DA, Chapman GD, Chute MD, Marston CK, De BK, Sacchi CT, Fitzgerald C, Mayer LW, Maiden MCJ, Priest FG, Barker M, Jiang L, Cer RZ, Rilstone J, Peterson SN, Weyant RS, Galloway DR, Read TD, Popovic T, Fraser CM. Identification of anthrax toxin genes in a Bacillus cereus associated with an illness resembling inhalation anthrax. *Proc Natl Acad Sci USA*. 2004;101(22):8449-8454.

DEPARTMENT OF HEALTH & HUMAN SERVICES

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NOV 1 8 2005

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Re: k051713
Trade/Device Name: JBAIDS Anthrax Detection System
Regulation Number: Unclassified
Product Code: NHT
Dated: September 29, 2005
Received: October 3, 2005

Dear Ms. Lingenfelter:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (240)276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
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Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K051713

Device Name: JBAIDS Anthrax Detection System

Indications For Use:

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The safety and effectiveness of other types of tests or sample types (not identified as "For in vitro diagnostic use") have not been established.

Prescription Use ___x___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K051713